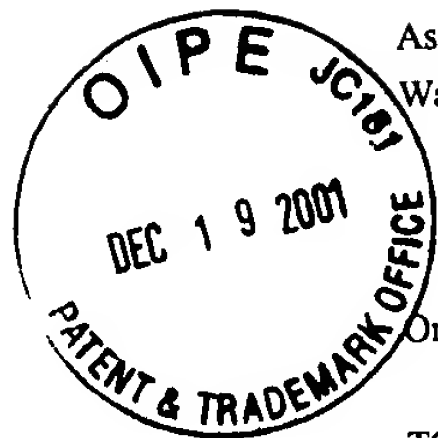


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PATENT  
Attorney Docket No.: 020031-000810US

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On December 7, 2001

TOWNSEND and TOWNSEND and CREW LLP

By: Debra Ann DeBello  
Debra Ann DeBello

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

John G.K. Williams

Application No.: 09/876,374

Filed: June 6, 2001

For: CHARGE-SWITCH  
NUCLEOTIDES

Examiner: Unassigned

Art Unit: Unassigned

INFORMATION DISCLOSURE  
STATEMENT UNDER 37 CFR §1.97 and  
§1.98

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

The references cited on attached form PTO/SB/08A and PTO/SB/08B are being called to the attention of the Examiner. Copies of the references are enclosed. It is respectfully requested that the cited references be expressly considered during the prosecution of this application, and the references be made of record therein and appear among the "references cited" on any patent to issue therefrom.

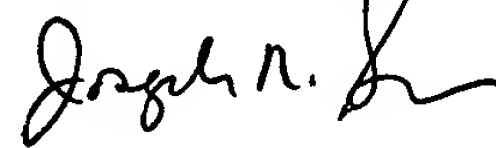
As provided for by 37 CFR 1.97(g) and (h), no inference should be made that the information and references cited are prior art merely because they are in this statement and no

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representation is being made that a search has been conducted or that this statement encompasses all the possible relevant information.

Applicant believes that no fee is required for submission of this statement, since it is being submitted prior to the first Office Action. However, if a fee is required, the Commissioner is authorized to deduct such fee from the undersigned's Deposit Account No. 20-1430. Please deduct any additional fees from, or credit any overpayment to, the above-noted Deposit Account.

Respectfully submitted,



Joseph R. Snyder

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: 925-472-5000  
Fax: 925- 472-5015  
JSIw

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

1

of

2

## Complete if Known

Application Number	09/876,374
Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	unknown
Examiner Name	unknown
Attorney Docket Number	020031-000810US

## U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code <sup>2</sup> (if known)			
	AA					
	AB					
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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	AU	WIPO	WO 98/28440		PYROQUENCING	07-02-1998		
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	AW							
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet

2

of

2

## Complete if Known

Application Number	09/876,374
Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	unknown
Examiner Name	unknown
Attorney Docket Number	020031-000810US

## OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AZ	TYAGI ET AL. Molecular Beacons: Probes that fluoresce upon Hybridization. <i>Nature Biotechnology</i> , March 1996, Vol 14, Page 303-308.	
	AAA	FU ET AL. A DNA Sequencing Strategy that Requires only Five Bases of Known Terminal Sequence for Priming. <i>Proc. Natl. Acad. Sci. USA</i> , October 1995, Vol. 92, Pages 10162-10166.	
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Sheet 1 of 8

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Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	
Examiner Name	
Attorney Docket Number	020031-000810US

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		Number	Kind Code <sup>2</sup> (if known)			
	AA	4,415,732		Caruthers <i>et al.</i>	11/15/83	
	AB	4,458,066		Caruthers <i>et al.</i>	7/3/84	
	AC	4,863,849		Melamede	9/5/89	
	AD	4,962,037		Jett <i>et al.</i>	10/9/90	
	AE	4,996,143		Heller <i>et al.</i>	2/26/91	
	AF	5,013,831		Stavrianopoulos	5/7/91	
	AG	5,047,519		Hobbs, Jr. <i>et al.</i>	9/10/91	
	AH	5,241,060		Engelhardt <i>et al.</i>	8/31/93	
	AI	5,405,747		Jett <i>et al.</i>	4/11/95	
	AJ	5,608,063		Hobbs, Jr. <i>et al.</i>	3/4/97	
	AK	5,635,608		Haugland <i>et al.</i>	6/3/97	
	AL	5,714,330		Brenner <i>et al.</i>	2/3/98	
	AM	5,723,591		Livak <i>et al.</i>	3/3/98	
	AN	5,800,996		Lee <i>et al.</i>	9/1/98	
	AO	5,846,737		Kang	12/8/98	
	AP	5,866,336		Nazarenko <i>et al.</i>	2/2/99	
	AQ	5,863,727		Lee <i>et al.</i>	1/26/99	
	AR	5,872,243		Gee <i>et al.</i>	2/16/99	
	AS	5,260,433		Engelhardt <i>et al.</i>	11/09/93	
	AT	5,332,666		Prober <i>et al.</i>	07/26/94	
	AU	6,191,266	B1	Wang	2/20/2001	
	AV	6,210,891	B1	Nyren <i>et al.</i>	4/3/2001	
	AW	6,232,075	B1	Williams	5/15/2001	
	AX	6,287,821	B1	Shi <i>et al.</i>	9/11/2001	

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### FOREIGN PATENT DOCUMENTS

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	AY	Europe	0272007	B1	Applied Biosystems, Inc.	03/04/92		

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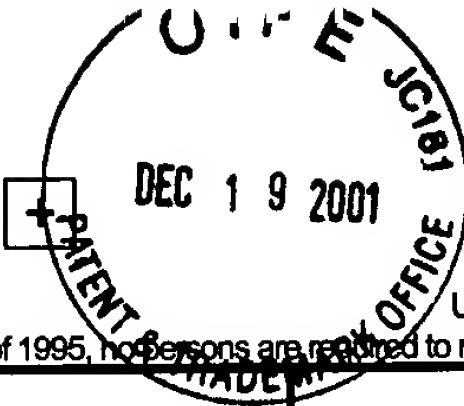
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Sheet

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### Complete if Known

Application Number	09/876,374
Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	
Examiner Name	
Attorney Docket Number	020031-000810US

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		Office <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)				
	AZ	WO	00/70073		Korlach <i>et al.</i>	11/23/2000		
	BA	WO	00/58507		Klenerman	10/05/2000		
	BB	WO	00/06770		Balasubramanian <i>et al.</i>	02/10/2000		
	BC	WO	00/27521		Balasubramanian <i>et al.</i>	05/18/2000		

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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 8

### Complete if Known

Application Number	09/876,374
Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	
Examiner Name	
Attorney Docket Number	020031-000810US

### OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

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	BD	Agrawal <i>et al.</i> , "Site-Specific Functionalization of Oligodeoxynucleotides For Non-Radioactive Labelling," <i>Tetrahedron Letters</i> , 31:1543-1546 (1990)	
	BE	Ambrose <i>et al.</i> , "Single-Molecule Detection With Total Internal Reflection Excitation: Comparing Signal-to-Background and Total Signals in Different Geometries," <i>Cytometry</i> , 36:224-231 (1999)	
	BF	Araki <i>et al.</i> , "Allosteric Regulation of a Ribozyme Activity Through Ligand-Induced Conformational Change," <i>Nucleic Acids Res.</i> , 26:3379-3384 (1998)	
	BG	Armstrong <i>et al.</i> , "Interaction of Substrate Analogues with <i>Escherichia coli</i> DNA-Dependent RNA Polymerase," <i>Eur. J. Biochem.</i> , 70:33-38 (1976)	
	BH	Asanov <i>et al.</i> , "Regenerable Biosensor Platform: A Total Internal Reflection Fluorescence Cell with Electrochemical Control," <i>Anal. Chem.</i> , 70:1156-1163 (1998)	
	BI	Bergstrom <i>et al.</i> , "Palladium-Mediated Coupling between Organic Disulfides and Nucleic Acid Constituents," <i>JACS</i> , 111:374-375 (1989)	
	BJ	Bonnaffe <i>et al.</i> , "Potential Lipophilic Nucleotide Prodrugs: Synthesis, Hydrolysis, and Antiretroviral Activity of AZT and d4T Acyl Nucleotides," <i>J. Org. Chem.</i> , 61:895-902 (1996)	
	BK	Castro <i>et al.</i> , "Single-Molecule Detection of Specific Nucleic Acid Sequences in Unamplified Genomic DNA," <i>Anal. Chem.</i> , 69:3915-3920 (1997)	
	BL	Church <i>et al.</i> , "Multiplex DNA Sequencing," <i>Science</i> , 240:185-188 (1988)	
	BM	Davis <i>et al.</i> , "Rapid DNA Sequencing Based Upon Single Molecule Detection," <i>GAIA</i> , 8(1):1-7 (1991)	
	BN	Eckstein <i>et al.</i> , "Phosphate Analogs for the Study of DNA Polymerases," <i>Methods in Enzymology</i> , 262:189-217 (1995)	
	BO	Edman <i>et al.</i> , "Conformational transitions monitored for single molecules in solution," <i>Proc. Natl. Acad. Sci. USA</i> , 93:6710-6715 (1996)	
	BP	Fleischmann <i>et al.</i> , "Whole-Genome Random Sequencing and Assembly of <i>Haemophilus influenzae</i> Rd," <i>Science</i> , 269:496-511 (1995)	
	BQ	Garcia, "Determination of Ion Permeability by Fluorescence Quenching," <i>Meth. Enzymol.</i> , 207:501-511 (1992)	

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Signature

Date  
Considered

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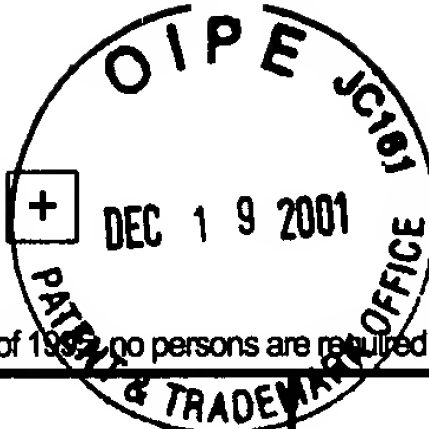
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## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 4 of 8

### Complete if Known

Application Number	09/876,374
Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	
Examiner Name	
Attorney Docket Number	020031-000810US

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	BR	Gebeyehu <i>et al.</i> , "Novel biotinylated nucleotide -- analogs for labeling and colorimetric detection of DNA," <i>Nucleic Acids Research</i> , 15:4513-4535 (1987)	
	BS	Gibson <i>et al.</i> , "Synthesis and application of derivatizable oligonucleotides," <i>Nucleic Acids Research</i> , 15: 6455-6467(1987)	
	BT	Giusti <i>et al.</i> , "Synthesis and Characterization of 5'-Fluorescent-dye-labeled Oligonucleotides," <i>PCR Methods and Applications</i> , 2: 223-227 (1993)	
	BU	Goody <i>et al.</i> , "The Enzymatic Synthesis of Thiophosphate Analogs of Nucleotides," <i>Biochem. Biophys. Acta.</i> , 276:155-161 (1972)	
	BV	Grachev <i>et al.</i> , "ATP $\gamma$ -Anilidate; A Substrate of DNA-Dependent RNA-Polymerase of <i>Escherichia Coli</i> ," <i>FEBS Lett.</i> , 49:163-166 (1974)	
	BW	Grachev <i>et al.</i> , "Studies on the functional topography of <i>Escherichia coli</i> RNA polymerase," <i>Eur. J. Biochem.</i> , 163:113-121 (1987)	
	BX	Griffin <i>et al.</i> , "Specific Covalent Labeling of Recombinant Protein Molecules Inside Live Cells," <i>Science</i> , 281:269-272 (1998)	
	BY	Gupta <i>et al.</i> , "A general method for the synthesis of 3'-sulfhydryl and phosphate group containing oligonucleotides," <i>Nucleic Acids Research</i> , 19:3019-3025 (1991)	
	BZ	Gyllensten <i>et al.</i> , "PCR-based HLA Class II Typing," <i>PCR Methods and Applications</i> , 1: 91-98 (1991)	
	CA	Haralambidis <i>et al.</i> , "Preparation of base-modified nucleosides suitable for non-radioactive label attachment and their incorporation into synthetic oligodeoxyribonucleotides," <i>Nucleic Acids Research</i> , 15: 4856-4876 (1987)	
	CB	Hobbs, "Palladium-Catalyzed Synthesis of Alkynylamino Nucleosides. A Universal Linker for Nucleic Acids," <i>J. Org. Chem.</i> , 54: 3420-3422 (1989)	
	CC	Hunkapiller <i>et al.</i> , "Large-Scale and Automated DNA Sequence Determination," <i>Science</i> , 254: 59-67 (1991)	

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Sheet 5 of 8

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	CD	Hyman, "A New Method of Sequencing DNA," <i>Analytical Biochemistry</i> , 174:423-436 (1988)	
	CE	Jett <i>et al.</i> , "High-Speed DNA Sequencing: An Approach Based Upon Fluorescence Detection of Single Molecules," <i>J. Biomol. Struct. Dyn.</i> , 7:301-309 (1989)	
	CF	Kadokura, M. <i>et al.</i> , "Efficient Synthesis of $\gamma$ -Methyl-Capped Guanosine 5'-Triphosphate as a 5'-Terminal Unique Structure of U6 RNA via a New Triphosphate Bond Formation Involving Activation of Methyl Phosphorimidazolidate Using $ZnCl_2$ as a Catalyst in DMF under Anhydrous Conditions," <i>Tetrahedron Letters</i> , 38:8359-8362 (1997)	
	CG	Kinjo <i>et al.</i> , "Ultrasensitive hybridization analysis using fluorescence correlation spectroscopy," <i>Nucleic Acids Res.</i> , 23:1795-1799 (1995)	
	CH	Köster <i>et al.</i> , "A strategy for rapid and efficient DNA sequencing by mass spectrometry," <i>Nature Biotechnology</i> , 14:1123-1128 (1996)	
	CI	Kreimeyer <i>et al.</i> , "Transmembrane Transport of Adenosine 5'-Triphosphate Using a Lipophilic Cholesterol Derivative," <i>Angew. Chem. Int. Ed.</i> , 37:2853-2855 (1998)	
	CJ	Kreimeyer <i>et al.</i> , "Synthesis of Acylphosphates of Purine Ribonucleosides," <i>Tetrahedron Letters</i> , 37:8739-8742 (1006)	
	CK	Laws <i>et al.</i> , "Fluorescence Quenching Studies: Analysis of Nonlinear Stern - Volmer Data," <i>Meth. Enzymol.</i> , 210:448-463 (1992)	
	CL	Li <i>et al.</i> , "Design, Synthesis, and Spectroscopic Properties of Peptide-Bridged Fluorescence Energy-Transfer Cassettes," <i>Bioconjugate Chem.</i> , 10:241-245 (1999)	
	CM	Luo <i>et al.</i> , "Fluorous Mixture Synthesis: A Fluorous-Tagging Strategy for the Synthesis and Separation of Mixtures of Organic Compounds," <i>Science</i> , 291:1766-769 (2001)	
	CN	Marshall, "Rules for the visible absorption spectra of halogenated Fluorescein dyes," <i>Histochemical J.</i> , 7:299-303 (1975)	
	CO	Maxam <i>et al.</i> , "A new method for sequencing DNA," <i>Proc. Natl. Acad. Sci. USA</i> , 74: 560-564 (1977)	

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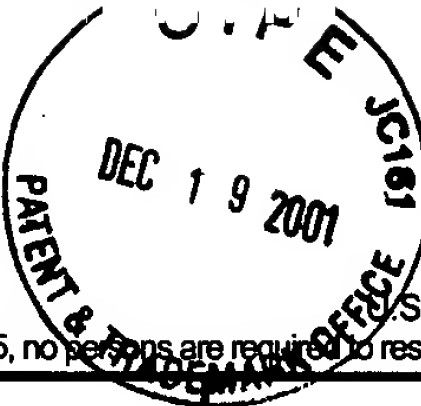
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Application Number	09/876,374
Filing Date	June 6, 2001
First Named Inventor	Williams, John G.K.
Group Art Unit	
Examiner Name	
Attorney Docket Number	020031-000810US

### OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS

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	CP	Narasimhan <i>et al.</i> , "p-Benzoquinone activation of metal oxide electrodes for attachment of enzymes," <i>Enzyme Microb. Technol.</i> , 7:283-286 (1985)	
	CQ	Nelson <i>et al.</i> , "Bifunctional oligonucleotide probes synthesized using a novel CPG support are able to detect single base pair mutations," <i>Nucleic Acids Research</i> , 17: 7187-7194 (1989)	
	CR	Nie <i>et al.</i> , "Probing Individual Molecules with Confocal Fluorescence Microscopy," <i>Science</i> 266:1018-1021 (1994)	
	CS	Nie <i>et al.</i> , "Real-Time Detection of Single Molecules in Solution by Confocal Fluorescence Microscopy," <i>Anal. Chem.</i> 67:2849-2837 (1995)	
	CT	Paris <i>et al.</i> , "Probing DNA sequences in solution with a monomer - excimer fluorescence color change," <i>Nucleic Acids Res.</i> , 26:3789-2393 (1998)	
	CU	Ronaghi <i>et al.</i> , "Sequencing Method Based on Real-Time Pyrophosphate," <i>Science</i> , 281:363-365 (1998)	
	CV	Sanger <i>et al.</i> , "DNA sequencing with chain-terminating inhibitors," <i>Proc. Natl. Acad. Sci. USA</i> , 74: 5463-5467 (1977)	
	CW	Sato <i>et al.</i> , "Bimane conjugates of 5-halogenouridylic acids as fluorogenic substrates for phosphodiesterase I," <i>J. Chem. Research (S)</i> , 1:390-391 (1994)	
	CX	Schecker <i>et al.</i> , "Flow-based continuous DNA sequencing via single molecule detection of enzymatically cleaved fluorescent nucleotides," <i>Proc. SPIE-Int. Soc. Opt. Eng.</i> 2386:4-12 (1995)	
	CY	Schmidt <i>et al.</i> , "Imaging of single molecule diffusion," <i>Proc. Natl. Acad. Sci. USA</i> 93, 2926-2929 (1996)	
	CZ	Service, "Borrowing from biology to power the petite", <i>Science</i> , 283:27 (1999)	
	DA	Smagowicz <i>et al.</i> , "Properties of P <sup>3</sup> Esters of Nucleoside Triphosphates as Substrates for RNA Polymerase from <i>Escherichia coli</i> ," <i>Biochem.</i> , 20:5538-5546 (1981)	

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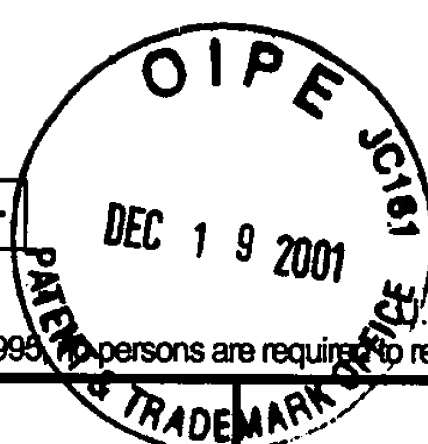
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	DB	Sproat <i>et al.</i> , "The synthesis of protected 5'-mercapto-2', 5'-dideoxyribonucleoside-3'-O-phosphoramidites; uses of 5'-mercapto-oligodeoxyribonucleotides," <i>Nucleic Acids Research</i> , 15:4837-4849 (1987)	
	DC	Steitz, "A mechanism for all polymerases," <i>Nature</i> , 391:231-232 (1998)	
	DD	Suto <i>et al.</i> , "Synthesis of $\gamma$ -phosphate-linked Nucleoside Affinity Chromatography Resins For Protein Purification, Including Ribonucleoside Triphosphate Reductase," <i>Nucleosides &amp; Nucleotides</i> , 17(8):1453-1471 (1998)	
	DE	Sverdlov <i>et al.</i> , "Derivatives of Guanosine Triphosphate-photoreactive Substrates of <i>Escherichia Coli</i> RNA Polymerase," <i>Elsevier/North-Holland Biomedical Press</i> , 112:296-298 (1980)	
	DF	Tokunaga <i>et al.</i> , "Single molecule imaging of fluorophores and enzymatic reactions achieved by objective-type total internal reflection fluorescence microscopy," <i>Biochem. and Biophys. Res. Comm.</i> , 235:47-53 (1997)	
	DG	Tyagi <i>et al.</i> , "Multicolor molecular beacons for allele discrimination," <i>Nature Biotechnol.</i> , 16:49-53 (1998)	
	DH	Velculescu <i>et al.</i> , "Serial Analysis of Gene Expression," <i>Science</i> , 270:484-487 (1995)	
	DI	Walker <i>et al.</i> , "Synthesis and Properties of Caged Nucleotides," <i>Methods in Enzymology</i> , 172:288-301 (1989)	
	DJ	Wang <i>et al.</i> , "Design and Synthesis of New Fluorogenic HIV Protease Substrates Based On Resonance Energy Transfer," <i>Tetrahedron Lett.</i> , 31:6493-6496 (1990)	
	DK	Weissleder <i>et al.</i> , "In vivo imaging of tumors with protease-activated near-infrared fluorescent probes," <i>Nature Biotechnol.</i> , 17:375-378 (1999)	
	DL	Wu <i>et al.</i> , "Synthesis and Properties of Adenosine-5'-triphosphoro- $\gamma$ -1-(5-sulfonic acid)naphthyl Ethylamidate: A Fluorescent Nucleotide Substrate for DNA-Dependent RNA Polymerase from <i>Escherichia coli</i> ," <i>Arch. Biochem. Biophys.</i> , 246:564-567 (1986)	

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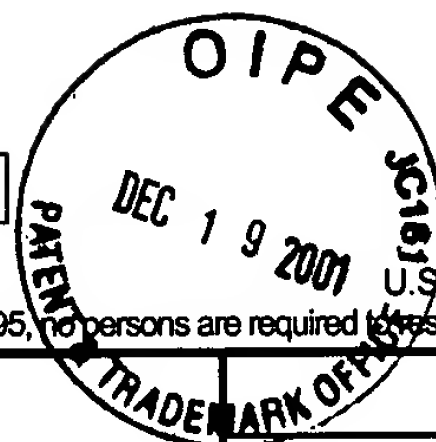
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	DM	Wu <i>et al.</i> , "An allosteric synthetic DNA," <i>Nucleic Acids Res.</i> , 1512-1516 (1999)	
	DN	Xu <i>et al.</i> , "Long-Range Electrostatic Trapping of Single-Protein Molecules at a Liquid-Solid Interface," <i>Science</i> , 281:1650-1653 (1998)	
	DO	Yarbrough <i>et al.</i> , "Synthesis and properties of fluorescent nucleotide substrates for DNA-dependent RNA polymerases," <i>JBC</i> , 254:12069-12073 (1979)	
	DP	Yarbrough <i>et al.</i> , "Stacking Interactions in Fluorescent Nucleotide Analogs Containing 1-Aminonaphthalene-5-Sulfonate at the Phosphoryl Terminus," <i>JBC</i> , 255:9907-9911 (1980)	
	DQ	Yarbrough <i>et al.</i> , "Binding of Fluorescent Analogs of GRP to the Exchangeable Nucleotide Binding Site of Tubulin," <i>JBC</i> , 256:112-117 (1981)	
	DR	Zuckermann <i>et al.</i> , "Efficient methods for attachment of thiol specific probes to the 3'-ends of synthetic oligodeoxyribonucleotides," <i>Nucleic Acids Research</i> , 15: 5305-5321 (1987)	
	DS	Livak <i>et al.</i> , "Oligonucleotides with Fluorescent Dyes at Opposite Ends Provide a Quenched Probe System Useful for Detecting PCR Product and Nucleic Acid Hybridization," <i>PCR Methods and Applications</i> , Cold Spring Harbor Laboratory Press., 4:357-362 (1995)	
	DT	Hunkapiller <i>et al.</i> , "Large-Scale and Automated DNA Sequence Determination," <i>Science</i> , 254:59-67 (1991)	
	DU	Griffin, <i>et al.</i> , "Specific Covalent Labeling of Recombinant Protein Molecules Inside Live Cells," <i>Science</i> , 281:269-272 (1998)	

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